

# **RISK FACTORS FOR MULTIDRUG-RESSISTANT TUBERCULOSIS IN ADDIS ABABA, ETHIOPIA**

by

**FIKADU TADESSE NIGUSSO**

Submitted in Accordance with the Requirements for the Degree of

**MASTER IN PUBLIC HEALTH**

at the

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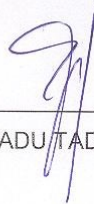
**SUPERVISOR: Dr NEGUSSIE TAFFA**

**November 2012**

Student number: 4677392-4

### Declaration

I declare that "RISK FACTORS FOR MULTI-DRUG RESISTANT TUBERCULOSIS IN ADDIS ABABA, ETHIOPIA" is my own work and that all the sources that I have used or quoted have been indicated and acknowledged by means of complete references and that this work has not been submitted before for any degrees at any other institution.



FIKADU TADESSE NIGUSSO

November 20, 2012

DATE

## *Dedication*

*I dedicate this study to the Almighty God, for his endless love, kindness, wisdom and grace that always abounds all the days of my life.*

*My dedication goes to my Grand Mom whose values of leadership, humility and sacrifice always remains fresh in my memory. My dedication also goes to my Grand Dad, may Your Soul Rest in Eternal Peace Dear Grand Pa!*

## **ACKNOWLEDGEMENTS**

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- To all my relatives and friends for always encouraging me to pursue my study.
- Last but not least, my special thanks go to my beloved fiancé Ayantu Belay who is always there supporting and encouraging me to complete my study.

# **RISK FACTORS FOR MULTI-DRUG RESISTANT TUBERCULOSIS IN ADDIS ABABA, ETHIOPIA**

STUDENT NUMBER: 4677-392-4

STUDENT: MR FT NIGUSSO

DEGREE: MASTER OF PUBLIC HEALTH

DEPARTMENT: HEALTH STUDIES, UNIVERSITY OF SOUTH AFRICA

SUPERVISOR: DR NEGUSSIE TAFFA

## **ABSTRACT**

This quantitative, descriptive study investigated risk factors for MDR-TB in Addis Ababa, Ethiopia. A total of 439 medical records belonging to MDR-TB and non MDR-TB patients managed in public health centres from January 2008 to December 2011 were analysed. Data were transcribed from each TB patient's medical records using a specifically designed checklist.

The findings revealed that male gender, previous history of TB treatment, poor treatment adherence, an outcome of failure after TB re-treatment, previous category of failure, pulmonary involvement of TB infection and HIV infection were associated with MDR-TB. The findings illustrate that efforts should be made to prioritise the development and implementation of effective MDR TB screening and treatment protocols for these high risk groups to improve treatment outcome and minimize the emergence of XDR TB.

### **Key Terms:**

Addis Ababa, MDR-TB, TB, risk factor, HIV

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**List of Abbreviations**

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AACAHB:	Addis Ababa City Administration Health Bureau
AFB:	Acid Fast Bacilli
AIDS:	Acquired Immuno-deficiency Syndrome
ART:	Anti-Retroviral treatment
DOTS:	Directly Observed Treatment Short Course
DST:	Drug Sensitivity Test
EHNRI:	Ethiopian Health and Nutrition Research Institute
FL-DST:	Full first line-DST
FMOH:	Federal Ministry of Health of Ethiopia
HIV:	Human Immunodeficiency Virus
GLC:	Green Light Committee
MDR:	Multidrug-Resistant
NTCP:	National TB Control Program
OAU:	Organization of African Unity
OPD:	Outpatient department
RHB:	Regional Health Bureaus
SLDs:	Second-line drugs
SL-DST:	second line DST
TB:	Tuberculosis
UNISA:	University of South Africa
WHO:	World Health Organization
XDR:	Extra drug-Resistant

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Annexure B- Permission Letter to Conduct the Research

Annexure C- Permission Letter from Addis Ababa City Administration Health Bureau

Annexure D- Data Abstraction Tool

## **CHAPTER 1**

### **Orientation to the study**

#### **1.1 INTRODUCTION**

Tuberculosis (TB) is one of the leading causes of morbidity, the fourth causes of hospital admissions, and the second cause of hospital deaths in Ethiopia (FMOH 2009). It has been recognized as a major public health problem since 1950. Since then control has been initiated by establishment of TB Sanatorium and latter strengthened by implementation of Directly Observed Treatment Short Course (DOTS) in the 1990s. Ethiopia has been implementing the WHO STOP-TB strategy since 2006. This strategy involves scaling up of effective chemotherapy and intensive health education for TB patients.

The continuous challenge in the occurrence and management of Multidrug-Resistant Tuberculosis (MDR-TB) in the country prompted this study which seeks-to investigate the risk factors for MDR-TB. Its outcomes are believed to help in designing appropriate prevention and control strategies. In doing so, results also indirectly improve our knowledge on Extensive Drug-Resistant Tuberculosis (XDR-TB) as the two share same contributing factors.

#### **1.2 BACKGROUND TO THE PROBLEM**

TB is a major global health problem. Globally, the absolute number of TB cases are increasing slowly, although the number of cases per capita (usually expressed as the number of cases per 100 000 population) is falling by around 1% per year. TB ranks as the eighth leading cause of death in low- and middle-income countries (seventh for men and ninth for women); among adults aged 15–59, it ranks as the third cause of death, after HIV/AIDS and ischemic heart disease. Each year, there are around 9 million new cases of TB, and close to 2 million people die from the disease. All countries are affected, but 85% of the



cases occur in Africa and Asia. Africa alone accounts 30% and Asia 55%, with India and China alone accounting for 35% of all cases for Asia (WHO 2010:7).

The most recent estimates of TB data from the World Health Organization (WHO), indicates that TB incidence declined in only 10 of 46 African countries between 2000 and 2007(WHO 2009a:5, 2010:32).

Global control of TB has been jeopardized by two major threats: HIV/AIDS and MDR-TB (multi-drug resistant tuberculosis). MDR-TB is defined as strains of *Mycobacterium tuberculosis* that are resistant to at least isoniazid and rifampicin (WHO 2008a:6).

Yet TB is, in most instances, a curable disease. Using combinations of first-line drugs introduced into treatment between the 1950s and 1980s, around 90% of people with drug-susceptible TB can be cured in six months. Treatment of MDR-TB of which there are around 0.4–0.5 million cases each year—is more challenging. It requires use of second-line drugs (including injectable antibiotics) that are more costly and cause more severe side-effects, and recommended regimens must be taken for up to two years. Cure rates for MDR-TB are lower, typically ranging from around 50% to 70%. Among TB patients globally notified in 2009, an estimated 250 000 (range, 230 000–270 000) had MDR-TB. Of these, slightly more than 30,000 (12%) were diagnosed with MDR-TB (WHO 2010:7).

Drug resistant tuberculosis develops as a result of mismanagement of susceptible TB. The mismanagement may include inappropriate treatment regimens (e.g., a wrong choice of drugs, dosage and duration of treatment), programme factors (e.g., irregular supply, incompetent health personnel), and patient factors (e.g., poor adherence i.e. patients may feel better and halt their medication, mal-absorption) (FMOH 2011: 17).

In Ethiopia, by 2008, WHO estimated the incidence MDR-TB among new TB cases to be 1.6 % (160 cases) and 11.8 % (5000 cases) among previously treated TB cases (WHO 2010b:17).

The Ethiopian Government has identified the MDR-TB as one of priority public health problems and initiated comprehensive treatment for MDR-TB cases in the country (FMOH 2011: 34, FMOH 2009: 6). One such measure includes endorsement of single procurement mechanisms for TB drugs and controlled use of second line anti-TB drugs since 2009.

### **1.3 GEOGRAPHICAL AREA**

The study was undertaken at health facility in Addis Ababa city. Addis Ababa is the capital city of Ethiopia. It is the largest city in Ethiopia, with a population of 3,384,569 according to the 2007 population census. Addis Ababa is a chartered city, has the status of both a city and a state. It is where the African Union and its predecessor the Organization of African Unity (OAU) are based. Addis Ababa is therefore often referred to as "The political capital of Africa", due to its historical, diplomatic and political significance for the continent. The city is populated by people from different regions of Ethiopia – the country has as many as 80 nationalities speaking 80 languages and belonging to a wide variety of religious communities. Addis Ababa lies at an altitude of 7,546 feet (2,300 meters) and is a grassland biome, located at 9°1'48"N 38°44'24"ECoordinates: 9°1'48"N 38°44'24"E(Encyclopaedia of the nation's 2011).

### **1.4 RATIONAL OF THE STUDY**

The study sought to examine the risk factors that contribute to emerging lethal problem of MDR-TB in Addis Ababa.

### **1.5 STATEMENT OF THE PROBLEM**

A problem statement articulates the problem to be addressed and indicates the need for a study (Polit and Beck 2007:65). Mosley (2008:4) describes a problem statement as "a statement that identifies the key research variables, specifies the nature of the population and suggests the possibility of empirical testing".

Ethiopia ranks 7<sup>th</sup> among the 22 high-burden countries and 15<sup>th</sup> in the list of 27 countries with the highest number of estimated MDR-TB cases (WHO 2009b). In a study conducted by Agonafir and his colleagues (2010) in Addis Ababa, MDR-TB was observed in one of the 44 new cases (2.3%) and 45/63 previously treated patients (71.4%). Despite the rising public health concern of MDR-TB in the country, factors underlying for spread of this diseases is not yet determined. Like most TB control programmes, the National Treatment Program does not have the resources to perform culture and drug susceptibility testing (DST) for all TB patients which is true for city of Addis Ababa (FMOH 2009:15). Consequently, the following questions were derived from the problem statement:

- What socio-demographic factors are associated with occurrence of MDR-TB in Addis Ababa?
- Is non-adherence to anti-TB treatment associated with development MDR-TB?
- Which types of TB treatment category and treatment outcomes are associated with multidrug-resistance?
- Is the emergence of MDR-TB associated with HIV/AIDS in Addis Ababa?

The problem that the researcher set himself is to make a demanding study on risk factors for spreading out of MDR-TB in Addis Ababa, Ethiopia. Once these factors are known and understood, a coherent strategy can be implemented to address the predicament of MDR-TB.

## **1.6 AIM OF THE STUDY**

The purpose of this study is to investigate risk factors for MDR-TB in Addis Ababa, Ethiopia.

### **1.6.1 Research objectives**

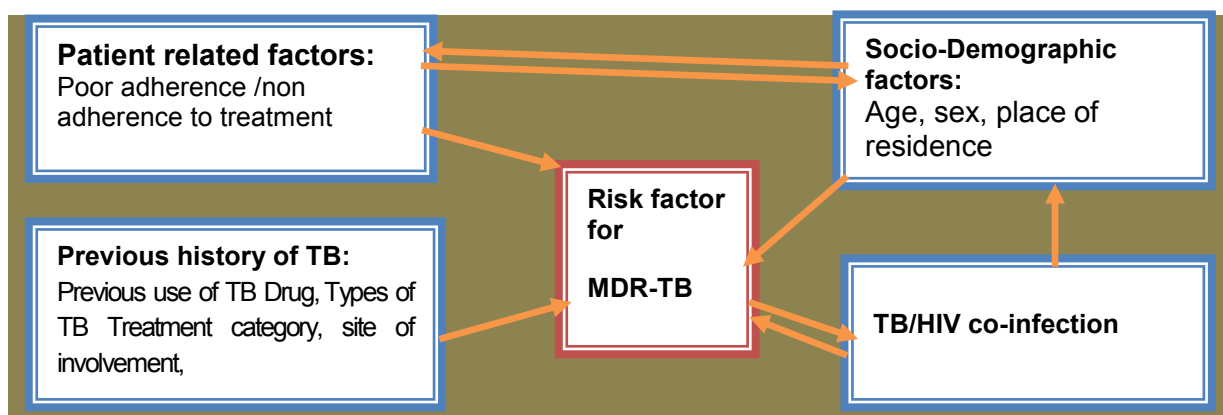
- To determine the socio-demographic factors associated with MDR-TB among patients in Addis Ababa.
- To determine if non adherence to treatment is associated with development MDR-TB.
- To determine the types of TB treatment categories and treatment outcomes associated with MDR-TB.
- To describe the association of HIV/AIDS and MDR-TB in Addis Ababa

## 1.7 SIGNIFICANCE OF THE STUDY

This study investigated the risk factors for MDR-TB in Addis Ababa, Ethiopia. Data on risk factors contributing for the occurrence of MDR-TB can be used in designing educational messages that can improve health care seeking towards MDR-TB. Study findings would have potential to encourage higher health officials to improve current TB control program shortcomings, as well as for conducting further research. Finally, the findings could provide important information on ways to improve quality of MDR-TB care in the country.

## 1.8 FOUNDATIONS OF THE STUDY

### 1.8.1 Conceptual framework of the study



**Figure 1.1 Conceptual framework of the study**

This conceptual framework is developed after an extensive review of pertinent literatures on MDR-TB in developing countries (W. S. Law, W. W. Yew, C.

Leung, K. M. Kam, C. M. Tam, C. K. Chan, C. C. Leung 2008:1065; Kliiman, K 2009: 66; L.A. Ferguson & J. Rhoads 2009:606). The variables included in the framework are believed to closely describe the realities experienced by most MDR-TB patients in Ethiopia. As could be seen in the figure, this study examined the problem of MDR-TB from four major angles namely the socio-demographic characteristics, patient behaviour, previous history of TB treatment and presence of HIV co-infection.

## **1.9 RESEARCH DESIGN AND METHODOLOGY**

### **1.9.1 Research design**

Polit and beck (2007:49) defines the study design as the overall plan for obtaining answers to the questions being studied and for handling some of the difficulties encountered during the research process. A research design is “an overall plan for collecting and analysing data, including specifications for enhancing the internal and external validity of the study” (De Vos, Strydom, Fouche & Delport 2002:137).

Cross-sectional comparative study design was employed for this study. The study characterizes MDR-TB patients and compares them with non MDR-TB patients on socio-demographic and patient related variables (risk factors).

### **1.9.2 Population**

A population is “an aggregate of people or objects with common characteristics of interest to the researcher” (Bowling 2002:157). In this study, the population of the study was all TB patients confirmed to be MDR and non MDR-TB patients in 26 public health centres in Addis Ababa from January 2008 to December 2011.

### **1.9.3 Sample and Sampling**

A sample is a subset of a population selected to participate in a study. Sampling is the process of selecting a portion of the population to represent the entire population. The selected elements are then referred to as the sample (De Vos et al 2002:198).

Risk of exposure to MDR-TB among newly confirmed TB patients was taken as an indicator variable in order to estimate the minimum number of cases that need to be sampled for the study. According to the Federal MOH of Ethiopia, the risk of MDR-TB among newly confirmed TB patients is nearly 2% compared to 12% among re-treated TB patients (FMOH 2009:3).

A Fleiss with Continuity Correction sample size calculation formula using Open Epi version 2.3 for windows were used to calculate the sample size. A marginal error of 3%, 80% study power, 95% confidence limit and a ratio of exposed (MDR) to unexposed (non-MDR) of 1:3 were assumed. Accordingly, a total of 400 study participants (100 MDR-TB and 300 non MDR-TB) were estimated to give sufficiently valid information to respond to the study questions. 10% of the samples were added to cater for incomplete data making the total sample size of 439 (113 MDR-TB and 326 non MDR-TB).

The researcher used a systematic random sampling method to select non MDR-TB patients registered in the 26 public health centres in Addis Ababa between January 2008 and December 2011 and fulfilling the selection criteria while all MDR patients seen in the 26 public health centres were included in the study. The number of non-MDR patients sampled from each health centre corresponded with TB case load and number of MDR-TB contributed from the site. TB registers were used as data source. From the registers found in each health centre, the ID numbers assigned to each patient seen between January 2008 and December 2011 were listed serially and every  $n^{\text{th}}$  non-MDR patient was selected for review until the required number of sample from the site is fulfilled.

#### **1.9.4 Data collection instrument**

The data was collected using a standard record review form adopted from the registry of national TB control program containing study variables.

#### **1.9.5 Data analysis**

The study was quantitative therefore both descriptive and analytic statistical methods were applied. The data were coded and entered in to Epi-Info version 3.5 and exported to SPSS version 16.0. The entered data were analysed by statistician. Odds ratio, chi-square test, and logistic regression were used for inferential statistics. Tables, graphs, charts, and percentages were used for descriptive statistics.

### **1.10. VALIDITY AND RELIABILITY**

#### **1.10.1 Validity**

To maintain the validity of the study, conceptual and operational definitions of terms were used according to the objective of the study. Records that meet eligibility and inclusion criteria based on clinical and laboratory results confirmed diagnosis were selected. Pre-tested data abstraction forms were used. The data were stratified for age and gender and multivariate analysis were performed during the analysis. Consultation with medical officers and nurses providing medical service for TB patients were done to measure the construct domain of the study to ensure instruments validity.

#### **1.10.2 Reliability**

To maintain the reliability of the study, careful training, development of a clearly defined standardized format after reviewing the literature, pre testing of the abstraction instrument and consulting experts in the field were designed and a small number of research assistants were used to enhance the accuracy of observer ratings and classifications. Only the researcher was responsible for

cleaning abstracted data and by so doing increased the chances of consistency in data collection.

### 1.11 ETHICAL CONSIDERATIONS

The goal of ethics in research is to ensure that no one is harmed or suffers adverse consequences from research activities. Chapter 3 discusses the ethical concerns fully.

### 1.12 DEFINITIONS OF KEY CONCEPTS

- ⊕ **Tuberculosis:** refers to all TB types that have been confirmed by clinical, AFB microscopy, culture (DST) and/or radiology.
- ⊕ **Multidrug-resistant tuberculosis (MDR-TB):** is defined as:
  - TB infection caused by strains of *Mycobacterium tuberculosis* that are resistant to at least isoniazid and rifampicin.
  - In this study, patients confirmed to be MDR and started his/her treatment and follow up at public health centres in Addis Ababa are included in the review.
- ⊕ **Non MDR-TB/sensitive TB cases** are all forms of TB which are sensitive to first line TB drugs.
- ⊕ **Extensively drug-resistant tuberculosis (XDR-TB):** is defined as MDR-TB plus resistance to a fluoroquinolone and at least one second-line injectable agent: amikacin, kanamycin and/or capreomycin.
- ⊕ **Non-adherence:** a patient is categorized as treatment non-adherent if they missed more than 20% of the prescribed doses during the intensive phase of the treatment period as recommended by WHO that can be confirmed from TB register of the patients. This same definition is applied in the current study.



- ⊕ **Cured:** patient is categorized as cured when a sputum smear becomes negative at, or one 'month' prior to, the completion of treatment (at 5<sup>th</sup> month).
- ⊕ **Treatment completed:** when a patient has completed the treatment course and smear results are not available at or one month prior to the completion of treatment.
- ⊕ **Defaulter:** Are when a patient has been on treatment for at least 4 weeks and whose treatment was interrupted for more than 8 consecutive weeks.
- ⊕ **Treatment failure:** is when a patient remains or becomes again smear-positive at 5 months or later during treatment.
- ⊕ **Drug resistance among new cases (Primary drug-resistance):** is a drug resistance in a patient who has never been treated for tuberculosis or received less than one month of therapy.
- ⊕ **Drug resistance among previously treated cases (Secondary or Acquired Drug-Resistance):** is a drug resistance in a patient who has received at least one month of anti-TB therapy.
- ⊕ **TB Treatment category:**
  - **Category I-** are TB treatment group for new and returnees after default from DOTS who have smear negative Pulmonary Tuberculosis (PTB).
  - **Categories II-** are the treatment category for the re-treatment cases including returns after default from DOTS who have smear positive.
  - **Category IV-** MDR-TB cases (still sputum positive after supervised re-treatment).

### 1.13 SCOPE AND LIMITATIONS OF THE STUDY

The study is limited by to its design which involved secondary analysis of clinical data. Secondary analysis of patient records has potential for deficiency in the amount of information required to answer the research objectives.

#### **1.14 OUTLINE OF THE STUDY**

This study has 5 chapters. Chapter 1 introduces the study and briefly outlines the problem, purpose and significance of the study, research design and methodology, and ethical considerations. Chapter 2 describes the literature review conducted for the study. Chapter 3 discusses the research design and methodology. Chapter 4 presents the data analysis and interpretation, and findings. Chapter 5 concludes the study and makes recommendations for practice and further research.

#### **1.15 CONCLUSION**

This chapter described the background to the problem, the purpose and significance of the study, the research design and methodology, as well as ethical considerations, and defined key terms. Chapter 2 discusses the literature review conducted for the study.

## CHAPTER 2

### Literature review

#### 2.1 INTRODUCTION

A literature review is undertaken to assist researchers to comprehend and extend their knowledge of the phenomenon under study (Polit & Beck 2008:105). Volmink (2007: 66) states that a literature review is indispensable if one wants to know (1) the current state of knowledge about any given subject, (2) what still needs to be studied so that the direction of future research can be efficiently determined, and (3) how available resources should be optimally allocated and distributed. This chapter discusses literature review conducted on risk factors for MDR-TB in Ethiopia and elsewhere.

*The literature review covered global epidemiology of MDR-TB, epidemiology of MDR-TB in Ethiopia, health care system of Ethiopia, TB prevention and control program in Ethiopia, and risk factors for MDR-TB.*

#### 2.2 GLOBAL EPIDEMIOLOGY OF MDR-TB

In 2008, an estimated 390 000–510 000 cases of MDRTB emerged globally (best estimate, 440 000 cases). Among all incident TB cases globally, 3.6% (95% confidence interval (CI): 3.0–4.4) are estimated to have MDR-TB. Almost 50% of MDR-TB cases worldwide are estimated to occur in China and India. In 2008, MDR-TB caused an estimated 150 000 deaths (WHO 2010a: 5; International council of nurses 2008: 19).

In 2007, the WHO reported the highest rates of MDR TB ever recorded, with up to 22% of new TB cases being resistant to both isoniazid and rifampicin in some areas of the former Soviet Union (WHO 2009b:4).

Seven drug susceptibility data were collected for 90,726 patients in 83 countries and territories from 2002 to 2007. The median prevalence of resistance in new cases of TB was 11.1% for any drug and 1.6% for MDR-TB. The prevalence of MDR-TB in new TB cases ranged from 0% in eight countries to 22.3% in Baku, Azerbaijan, and 19.4% in the Republic of Moldova. Of the 20 settings with the highest proportion of MDR-TB in new cases, 14 are located in countries of the former Soviet Union (between 6.8% and 22.3% in nine countries, including Moldova and Azerbaijan) and four in China (7% in two provinces in China) (Wright A, Zignol M, Van Deun A, et al.2009: 373; WHO 2008a: 120).

Countries conduct surveillance of anti-TB drug resistance as component of any TB control programme with four main objectives: a) measure the burden of drug-resistant TB and accurately plan treatment programmes with second-line drugs; b) assess epidemiological trends as a reflection of the effectiveness of implemented drug-resistant TB prevention and control activities; c) design effective empirical, standardized regimens for the treatment of TB, particularly for patients who have already been treated for TB and return with the disease; and d) promptly identify local outbreaks of drug-resistant TB in order to respond in a timely way (WHO 2011:14).

## **2.3 EPIDEMIOLOGY OF MDR-TB IN ETHIOPIA**

Ethiopia ranks 7<sup>th</sup> in the list of the world's 22 high burden countries for TB with incidence estimated at 379/100,000 for all forms of TB and 168/100,000 for smear positive tuberculosis. The Annual Risk of TB Infection is estimated at 2.2% (FMOH 2009:1). WHO 2011 TB report estimates 2,400 new MDR-TB cases every year in Ethiopia.

The first study on primary and initial drug resistance of *Mycobacterium Tuberculosis* in Ethiopia was reported in 1984. The study showed primary resistance to Isoniazid and Streptomycin to be 14.8% and 4.9%, respectively. Several studies were done later in Addis Ababa and in some other parts of the country with results showing primary or initial drug resistance to one or more drugs ranging from 7.6% to 32.5% (FMOH 2007:23).

According to the anti-TB drug resistance survey conducted nationwide in 2005 by the Ethiopian Health and Nutrition Research Institute (EHNRI), among 804 newly diagnosed TB cases, 1.6% were found to be infected with MDR-TB. The rate of MDR-TB among specimens from 76 previously treated TB cases was 11.8%. Based on the prevalence rate from the survey and TB case notification in 2007/08, the magnitude of MDR-TB in Ethiopia was estimated to be 997 cases, which includes 651 and 346 MDR-TB cases among newly diagnosed and re-treatment cases respectively.

According to WHO 2008 report, in Ethiopia, 5,825 MDR-TB cases (4964 among newly diagnosed and 861 among previously treated TB cases) were estimates to have occurred in 2006 (WHO 2008a:12). In addition, based on the prevalence rate from the survey and TB case notification in 2007/08, the magnitude of MDR TB in Ethiopia was estimated to be 997 cases, which includes 651 and 346 MDR-TB cases among newly diagnosed and re-treatment cases respectively (FMOH 2009:2).

## **2.4 HEALTH CARE SYSTEM OF ETHIOPIA IN RELATION TO TB**

The healthcare delivery system in Ethiopia emphasises primary healthcare (PHC), including preventive, promotive and basic curative services which involves prevention and control of diseases, including TB (FMOH 2007:14).

The government of Ethiopia recently introduced a three-tier health care delivery system which is characterized by a first level of a Woreda/District health system comprising a primary hospital (with population coverage of 60,000-100,000 people), health centres (1/15,000-25,000 population) and their satellite health posts (1/3,000-5,000 population) that are connected to each other by a referral system. A primary hospital, health centres and health posts form a primary health care unit (PHCU) with each health centre having five satellite health posts. The second tier is a general hospital with population coverage of 1-1.5 million people; and the third tier a specialized hospital that covers population of 3.5-5 million. Health management offices at different levels of the health sector

include the Federal Ministry of Health, Regional State Health Bureaus and Woreda Health Offices (one of the administrative unit below zonal level and above district/kebele level). Health Offices are responsible for financial and program planning, decision making in management and coordination, supervision, and quality assurance. The FMOH and the Regional Health Bureaus (RHB) focus more on policy matters and technical support while Woreda Health Offices have basic roles of managing and coordinating the operation of a district health system under their jurisdiction. Regions and districts have RHBs and district health offices, respectively for the management of public health services at their levels. The devolution of power to regional governments has resulted in the shifting of decision making for public service deliveries from the centre to largely under the authority of the regions and down to the district level (FMOH 2010:4).

A National TB Control Program (NTP) is in charge of all TB control activities and implementation guidelines following the DOTS principles. Task and responsibilities at Federal and Regional State Health Management Offices are clearly defined. However the MDR-TB program of the NTP needs to be tailored to the Regional State situation, based on local MDR-TB epidemiology, infrastructure and taking into account cultural specifics. Therefore, the programmatic management of MDR-TB in Ethiopia is introduced in a stepwise manner, starting with a Green Light Committee approved pilot program in Addis Ababa. Nevertheless, a rapid expansion to the regions is foreseen and preparation is underway (FMOH 2009:3).

## **2.5 TB PREVENTION AND CONTROL PROGRAM IN ETHIOPIA**

Tuberculosis prevention and control has been established from the time where TB has identified as one of the major public health problem in Ethiopia since about 5 decades. The effort to control tuberculosis began in the early 1960s with the establishment of TB centres and sanatoriums in three major urban areas in the country. These centres practically had not significant impact on reducing the burden of the disease in the country. The Central Office of the National Tuberculosis Control Programme was established in 1976. In 1992 a

standardised and well-organised TB programme, incorporating directly observed short course treatment, was implemented in a few pilot areas of the country (FMOH 2007:14). At present, tuberculosis control strategy in Ethiopia, relies on WHO recommended Stop TB Strategy and it has been implemented in the country since 2006 (FMOH 2009:1).

In 2006, the World Health Organization (WHO) launched the *Stop TB Strategy* as the internationally-recommended approach to reducing the burden of TB in line with global targets set for 2015. The goal of the strategy is defined as: “To dramatically reduce the global burden of TB by 2015 in line with the Millennium Development Goals and the Stop TB Partnership targets.”

It is of utmost importance that drug-resistant TB be prevented by rigorous adherence to the principles of the National Tuberculosis Control Programme (the DOTS strategy) and by patiently and consistently building partnerships with patients, their families and communities to cure TB at the first attempt (FMOH 2009:3). Ethiopia has been implementing this WHO STOP-TB strategy since 2006.

In order to reach the national objectives and targets, the TB Control Program of Ethiopia is aligned with the globally recommended Stop TB Strategy which includes: 1) Early case detection, 2) Adequate chemotherapy, 3) Provision of comprehensive & standard patient care, 4) Enhanced case management, 5) Accurate Monitoring and Evaluation (M & E) of program performance, and 6) Community participation FMOH (2008:13). At peripheral level, TB is integrated within the general health care services. In a typical health facility, both laboratory personnel and outpatient department (OPD) staff are most of the time also in charge of other health activities.

### **2.5.1 MDR-TB Prevention and Control in Ethiopia**

(FMOH 2009: 4) the government of Ethiopia adopted the five components of the DOTS Strategy as prevention and control of drug resistant TB: 1) Sustained political commitment by addressing the factors leading to the emergence of

MDR-TB, long-term investment of staff and resources, coordination of efforts between communities, local governments and international agencies, and a well-functioning DOTS programme. 2) Appropriate case-finding strategy including quality-assured culture and drug susceptibility testing (DST) in triage of patients into DST and the Drug-Resistant TB control programme in enhancing relationship with supranational TB reference laboratory. 3) Appropriate treatment strategies that use second-line drugs under proper case management conditions with rational treatment design (evidence-based), DOTS, monitoring and management of adverse effects, and properly trained human resources. 4) Uninterrupted supply of quality-assured second-line anti-tuberculosis drugs. 5) Recording and reporting system designed for drug resistance-TB control programs that enable performance monitoring and evaluation of treatment outcomes.

## **2.6 MDR-TB TREATMENT STRATEGIES IN ETHIOPIA**

Compared with therapy for drug susceptible tuberculosis, treatment of MDR-TB requires a longer duration, is considerably more complicated, expensive, and toxic, and treatment success rates are typically lower (Marahatta, SB. 2010:122).

General principles for designing a regimen for treatment of highly drug resistant TB are: 1) use of at least four drugs, whose effectiveness is highly likely or certain, 2) avoidance of drugs for which resistance crosses over, 3) elimination of drugs that are not safe for the patients, 4) inclusion of drugs from the following groups: a) first-line anti-TB drugs, b) injectable anti-TB agents c) fluoroquinolones, d) oral bacteriostatic second-line anti-TB drugs, and e) anti-TB agents with un clear efficacy in a hierarchical order based on the potency, and 5) preparedness to monitor, prevent and manage adverse effects for each of drugs selected (Matteelli, A, Migliori, GB, Cirillo, D, Centis, R, Girard, E, Raviglion, M. 2007;5:857-871).

The TB Control Program in Ethiopia did not start managing MDR-TB cases with efficient second line protocols until 2009 (FMOH (2009:3).



The Ethiopian MDR-TB treatment strategy combines standardised and individualized treatment based on second line DST (kanamycin and Ofloxacin) in all confirmed MDR-TB patients. All MDR-TB suspects will be referred for line probe assay, followed by full first line-DST (FL-DST) and partial second line DST (SL-DST) once MDR-TB is confirmed. Whereas all known MDR-TB patients will have FL-DST and SL-DST performed simultaneously. Line probe assay will assist in the decision to start the standard second line anti-TB treatment. Standardised regimens will be given to all confirmed MDR-TB cases under daily DOT (at least one drug intake will be medically supervised per week daily). The initial phase will be at least six months, and then the continuation phase will be at least 12 months. The total duration may be extended by clinicians according the findings of culture conversion. Treatment will be adjusted after receiving FL-and SL-DST result according to regimens (FMOH 2009:47-48).

In Ethiopia, the standard regimen for MDR-TB is: [Ethambutol- Pyrazinamide – Kanamycin (Amikacin)– Levofloxacin – Ethionamide – Cycloserine] for six months, and [Ethambutol – Pyrazinamide – Levofloxacin – Ethionamide – Cycloserine] for 12 months (FMOH 2009: 32-33) .

Management of MDR-TB cases is coordinated by St. Peter TB Specialized Hospital in the city of Addis Ababa (FMOH 2009:5) which has the right clinical expertise and experience with managing the second line anti-TB drugs and their side effects. This Hospital functions as a national referral centre in case of severe side effects and as a centre of excellence and training during the scaling up to the regions.

The All Africa Leprosy Rehabilitation and Training Center (ALERT) has recently begun contributing its share in treating MDR-TB patient since December 2011. The opening of the center has increased the number of MDR-TB treatment centers in Ethiopia to three. The other two are St. Peter's TB Specialized Hospital in Addis Ababa and Gonder University Hospital in Amhara Regional State. Besides, the Ministry has made preparations to open new MDR-TB diagnostic laboratories in Mekelle, Adama, Hawassa and Bahir Dar towns in

addition to existing two in Addis Ababa (<http://www.ertagov.com/erta/erta-news-archive/37-erta-tv-top-news-addis-ababa-ethiopia/1434-mdr-tb-diagnostic-labs-treatment-centers-to-be-expanded-to-regional-towns-.html>)

## **2.7 RISK FACTORS FOR MDR-TB**

Drug resistant tuberculosis develops as a result of mismanagement of susceptible TB. The mismanagement may include inappropriate treatment regimens (e.g., a wrong choice of drugs, dosage and duration of treatment), programme factors (e.g., irregular supply, incompetent health personnel), and patient factors (e.g., poor adherence i.e. patients may feel better and halt their medication, mal-absorption) (FMOH 2011: 17). In fact, it could be said that the occurrence of MDR-TB itself is an evidence of systematic failure of the community to tackle a curable diseases (Singh, JA, Upshur, R, and Padayatchi, N. 2007:0023). Previous treatment, age group between 25-44 year and less than 65 years, TB/HIV co-infection, poor living conditions, poverty and malnutrition, homelessness, alcohol abuse, prisons and overcrowding are the risk factors for MDR-TB (Kliiman, K. 2009: 66).

The increase in prevalence and incidence of MDR TB are caused by concurrent factors such as inadequate treatment regimens, poor case holding, suboptimal drug quality and transmission of resistant strains (WHO 2008b: 11).

### **2.7.1 Previous history of tuberculosis treatment**

Previous history of anti-tuberculosis treatment is the most widely reported risk factor for MDR-TB. Previously treated TB has strongest association with MDR-TB in addition to the duration of previous TB treatment (Kiliman, K. 2009:64). Patients who received previous anti-tuberculosis treatment had a 4-fold increased odds of multidrug resistance (OR, 4.11 [CI, 2.77 to 6.08] (Kai, K, Altraja, A. 2009: 770; Alistair, D, Calver, Alecia, A, Falmer, Megan, M, Odelia, J, Strauss, Elizabeth, M, Streicher, Madelene, H, Thelma, L, Mothusi, M, Paul, D, Helden, V, Robin, M, Warren, and Thomas C. Victor 2010: 268).

Prior exposure to anti-TB drugs is a well-established risk factor for drug resistance, as shown from surveys and surveillance systems worldwide (WHO 2010:10). Previously treated TB cases, however, are a heterogeneous group composed of relapse cases (that is, patients in whom TB has recurred after successful treatment), cases having failed one or more treatment regimens using first-line and/or second-line drugs, cases returning after treatment default, and others.

The high proportion of MDR-TB among new TB cases could suggest suboptimal infection control, whilst the high percentage of MDR-TB among retreatment cases suggest poor case holding and follow-up or suboptimal use of TB regimens (Ködmön, C, Hollo, V, Huitric, E, Amato-Gauci, A, and Manissero, D. 2010:4).

In a study conducted in South Africa, nearly 30% of MDR-TB patients had no previous treatment for tuberculosis, and few had received more than one previous treatment regimen (Jason R. Andrews, N. Sarita Shah, Darren Weissman, Anthony P. Moll, Gerald Friedland, Neel R.Gandhi 2010:4).

#### ***2.7.1.1 Types of previous TB treatment category***

In a study conducted in urban metropolis of Mumbai in Western India, 301/493 (60%) of MDR-TB patients are among the first line treatment-failures (D'souza et al 2009: 9). Failure of re-treatment regimens and chronic TB cases, relapse, return after default and failure of first-line short course chemotherapy are among the risk factors for MDR-TB (FMOH 2009:15). C-Y Chiang et al (2010: 418) the proportion of drug-resistant TB among previously treated TB cases consist of relapse, treatment after default, treatment after failure varied considerably in different settings depending on the prevalence of primary resistance.

#### ***2.7.1.2 Previous TB treatment outcome***

In the study done at Edendale Hospital in KwaZulu-Natal, Republic of South Africa showed that there is an association between treatment failure and any drug resistance of patients being re-treated for TB. TB treatment failure as outcome of previous treatment was associated with a 50-fold increase in risk of having MDR or XDR TB and was the most common re-treatment status among patients with MDR and XDR TB (Schreiber, Y, Herrera, A, Wilson, D, Wallengren, K, Draper, R, et al. 2009: 13: 1274–1280). Another study conducted in the same country compared the MDR and XDR-TB cases with drug susceptible TB controls, MDR and XDR-TB were strongly associated with a history of TB treatment failure (OR 51.7 [CI 6.6–403.7] (Andrews JR, Shah NS, Weissman D, Moll AP, Friedland G, et al.2010:4).

A high proportion of MDRTB and poly-resistance, 41% (95/231) and 26% (59/231) respectively, was observed in a study conducted in India by D'souza and his colleagues (2009) amongst the first line treatment-failures. A descriptive, case-series study conducted on MDR-TB patients registered for DOTS-Plus treatment at Bhim Hospital- the Rupandehi district hospital at Bhairahawa, Nepal showed Out of the total MDR-TB study subjects, 4 (13%) had been marked as defaulters and as many as 4/5<sup>th</sup> of the patients had had an incomplete treatment of TB. The remaining 1/5<sup>th</sup> had treatment failure in spite of not missing a single dose of drug during the previous treatment (Pant, R, Pandey, KR, Joshi, M, Sharma, S, Pandey, T, Pandey, S 2009:90).

### **2.7.2. TB/HIV Co-infection**

Recent global data have shown rising rates of drug-resistant TB in sub-Saharan Africa, the region also suffering from the world's highest burden of HIV/AIDS (WHO 2010: 6). MDR-TB is associated with HIV infection. The percentage of MDR-TB among HIV infected individuals was found to be three times higher (kiliman 2009:67). Among 136 suspected cases of MDR-TB, HIV-infection was confirmed among 114 in South Africa (88%) (Scott K Heysell, Tania A Thomas, Neel R Gandhi, Anthony P Moll, François J Eksteen, Yacoob Coovadia, Lynette Roux, Palav Babaria, Umesh Laloo, Gerald Friedland, Sarita Shah 2010:3).

Another study conducted at Tugela Ferry, KwaZulu-Natal province, South Africa, showed that among those ever tested for HIV infection, 90% of patients with MDR TB were co-infected with HIV (Gandhi, Shah, Andrews, et al.2010:82). But in a systematic review of studies that assessed HIV infection as a risk factor for MDR-TB (Suchindran, S, Brouwer, ES, Van Rie, A. 2009:4), association between MDR-TB and HIV or acquired MDR-TB and HIV was not demonstrated, but there was suggestion that HIV infection is associated with primary MDR-TB. However, based on the current data, HIV-positive TB patients in three Eastern European countries (Estonia, Latvia and the Republic of Moldova) appear to be more at risk of harbouring MDR-TB strains.

In Lithuania, where drug resistance data could not be disaggregated by HIV-negative and unknown HIV status, HIV-positive TB patients had a 8.4 (95% CI: 2.7–28.2) times higher odds of harbouring MDR-TB strains than TB patients for whom HIV status was unknown, indicating a possible association of the two epidemics (WHO 2010:14). According to current hypotheses HIV increases the chances of transmission of MDR-TB rather than leading to an inadequate treatment (WHO 2008). However the study conducted in Nepal by Pant, R, Pandey, KR, Joshi, M, Sharma, S, Pandey, T, Pandey, S (2009:91) showed that only 2 out of the 31 MDR-TB patients tested positive for HIV. The other 29 had a negative test indicating HIV positive status and MDR may be events independent of each other.

### **2.7.3 Age and MDR-TB**

In a surveillance data collected from 13 countries of Central and Eastern Europe, the frequency of MDR-TB was much higher in all age groups compared with the rest of the countries (all high-income) and peaked in young adulthood. In the high-income non-Central and Eastern Europe group, frequency of MDR-TB declined linearly with age-group ( $p < 0.05$ ). This pattern suggests that in the countries of the former Soviet Union, where many MDR-TB cases are of local origin, the MDR-TB epidemic is a relatively recent phenomenon and bears the highest toll on young adults (WHO 2010:4).

Younger age is known to be the significant contributor for development of MDR-TB (W. S. Law et al. 2008:1065). Contrary to this, the study conducted in South Africa showed that age was not a significant risk factor, it was found that MDR-TB was cultured from the blood in patients as young as 8 years and as old as 62 years (Scott et al. 2010:3).

D'souza et al (2009: 9) reported a significantly higher proportion of failures (MDR cases) in the age group of 36–55 years as compared to those whose strains were sensitive/mono-resistant ( $p < 0.022$ ). A significantly higher number of treatment-failures were MDR as compared to the new cases ( $p = 0.0$ ).

#### **2.7.4 Sex and MDR-TB**

According to WHO (2010) drug resistance surveillance report, among 38 countries and 3 territories the odds ratio of harbouring MDR-TB strains for female TB cases compared with male TB cases was 1.1 (95% CI: 0.9–1.4), showing no overall association between MDR-TB and sex of the patient. In South Africa, although a higher number of male than female MDR-TB cases were reported (4826 vs 4615 cases, respectively), data from a total of 81,794 TB patients with known sex (95% of all patients) indicates that female TB cases have a 1.2 times higher odds of harbouring MDR-TB strains than male TB cases. Data from Australia, the Netherlands and the United States of America also show a higher risk of MDR-TB in female patients (WHO 2010:12).

In a study conducted in Peru among 673 patients, more than half of diagnosed and confirmed (60.8%) MDR-TB were male which shows that gender is a risk factor for the development of MDR-TB (Molly F. Franke, Sasha C. Appleton, Jaime Bayona, Fernando Arteaga, Eda Palacios, Karim Llaro, Sonya S. Shin, Mercedes C. Becerra, Megan B. Murray, and Carole D. Mitnick 2008:4).

In a systematic review conducted by A Faustini, A J Hall, C A Perucci (2006:161) there was a stronger association of being a male sex as a risk factor for MDR-TB (OR 1.54; 95% CI 1.31 to 1.82) in the eight studies carried out in Western Europe and heterogeneity between studies were very low

( $p=0.956$ ). Men were at lower risk of MDR-TB in the three studies carried out in the former USSR (OR 0.86; 95% CI 0.43 to 1.71) with a high heterogeneity between studies ( $\chi^2=6.53$ ;  $p=0.04$ ).

#### **2.7.5 Poor TB Treatment Adherence**

Non-adherence to prescribed treatment is often underestimated. Poor compliance with treatment is also an important factor in the development of acquired drug resistance. Poor adherence were related to age differences as younger patients are often occupied by study, work or other activities on a daily basis, in contrast with the more sedentary lifestyle post-retirement age (W. S. Law et al. 2008: 1066). 1/5<sup>th</sup> TB patients had developed treatment failure as an outcome of TB treatment in Nepal in spite of not missing a single dose of drug during the previous treatment (Pant, R, Pandey, KR, Joshi, M, Sharma, S, Pandey, T, Pandey, S 2009:90), showing that poor or good adherence to therapy is not linked to the emerging problem of MDR-TB.

#### **2.7.6 Site of TB Involvement**

In a study conducted in Hong Kong, the vast majority of MDR-TB cases suffered from pulmonary TB (PTB) (98%), and only 2% presented with extra-pulmonary TB (EPTB) alone (W. S. Law et al. 2008: 1066). On the contrary, a study conducted in South Africa showed that approximately one quarter of drug resistant TB patients were diagnosed with extra-pulmonary TB in addition to pulmonary TB (Andrews et al.2010:3). Another study conducted in Tomsk, Russian Federation, discloses that sputum-smear positivity was significantly associated with MDR-TB (IY Gelmanova, S Keshavjee, VT Golubchikova, VI Berezina, AK Strelis, GV Yanova, S Atwood & M Murray 2007:705).

## **CHAPTER 3**

### **Research Design and Methodology**

#### **3.1 INTRODUCTION**

Research methodology is the approach or the design that is followed by a researcher to answer a particular research question. As described by Burns and Grove (2005:211), research methodology is the strategy that will be applied in a process that begins with the identification of the research problem and ends with plan of data collection. This research was done using a quantitative, descriptive and comparative cross-sectional research design. Data were collected using checklist which was designed to align with the national TB registration log-book in order to collect the study variables through medical record reviews.

This section covers the design of the study, how the sample was selected, the setting where the study was conducted, the study population, inclusion and exclusion criteria used during the study.

#### **3.2 STUDY DESIGN**

Polit and beck (2007:49) defines the study design as the overall plan for obtaining answers to the questions being studied and for handling some of the difficulties encountered during the research process. A research design is a blueprint for conducting the study that maximizes control over factors that could interfere with the validity of the findings (Burns & Grove 2005:211). A research design is a plan indicating how the study is going to be carried out. It is a plan guide for providing sound answers to a research questions. The study design guides what type of observations, and which measurement instrument will be adopted and when to conduct the data collection (Stommel & Wills 2004:32-34).



The research design followed for this study is comparative cross-sectional study design. The objective of the study was to determine the risk factors contributing for the occurrence of MDR-TB in Addis Ababa, Ethiopia.

### **3.2.1 Quantitative**

In quantitative research, evidence is gathered according to a specified plan, using formal instruments to collect the needed information (Somekh & Lewin 2005:215). Max Mmuya (2007:80) defined quantitative research as “a formal, objective, systematic process in which numerical data are utilized to obtain information about the world”.

This study reviewed medical records of MDR-TB patients and compared their information with non-MDR-TB patients to determine the risk factors for MDR-TB.

### **3.2.2 Descriptive study**

Polit and Beck (2007:193) descriptive studies is to observe, describe, and document aspects of a situation as it naturally occurs and sometimes to serve as a starting point for hypothesis generation or theory development. It is the study which seeks to document the characteristics, prevalence, intensity, or full nature of phenomena. Descriptive designs help to identify problems in current practice with a view to improve practice outcomes (Burns and Grove 2005:248). The study determines differences between the two groups (MDR-TB and non MDR-TB patients) and provides detailed analysis of the risk factors for emerging problem of MDR-TB in Addis Ababa.

### **3.2.3 Cross-sectional Research Design**

A study design in which data are collected at one particular point in time is called a cross-sectional research design (Polit & Beck 2008: 751). As described by Stommel and Wills (2004:159) a cross-sectional study is a study which collects information at a single point in time. A cross-sectional research design

assesses and describes the prevalence of the outcome or the extent of the exposure of a population to a predetermined phenomenon. The sample in a cross-sectional study is assembled randomly without any reference to exposure or outcome. The researcher then compares the outcome with the exposure, and tries to determine whether there is a difference in the prevalence of the outcome when it is compared to the exposure of the population (Morrone & Myer 2007: 85).

According to Burns and Grove (2005:236), cross-sectional study designs examine participants simultaneously, irrespective of their stage of development but with an aim to describe differences in phenomena across stages. Data is collected at a point in time but with different study participants, as opposed to different points in time for the same participant (Brink 2007:10).

#### **3.2.4 Comparative studies**

Comparative studies are used to examine existing differences between variables in two or more groups in their natural uncontrolled setting, and the results are not usually generalisable (Burns & Grove 2005:730).

### **3.3. SAMPLING**

Sampling is a process of selecting a portion of population, which is an entire aggregate of cause (Polit and Beck 2008:362). Sampling involves a process of selecting a sub-set of a population which represents the entire population in order to obtain characteristics of a particular phenomenon. A sample is the sub-set of cases or observations drawn from a population, who fulfilled the eligibility criteria participated in the study. There are two methods of sampling; one yields probability sampling in which the probability of selection relies on random selection process and the other is the non-probability sampling where sample selection does not follow random selection procedures (Stommel & Wills 2004:297-300).

The researcher used a systematic random sampling method to select non MDR-TB patients registered in the 26 public health centres in Addis Ababa between January 2008 and December 2011 and fulfilling the selection criteria while all MDR patients seen in the 26 public health centres were included in the study. A total of 113 MDR-TB patients were registered in these 26 public health centers during the period. The number of non-MDR patients sampled from each health centre corresponded with TB case load and number of MDR-TB contributed from the site. TB registers were used as data source. From the registers found in each health center, the ID numbers assigned to each patient seen between January 2008 and December 2011 were listed serially and every  $n^{\text{th}}$  non-MDR patient was selected for review until the required number of sample from the site is fulfilled.

This means that each individual in the non-MDR TB population followed at the 26 public health centers had fairly equal chance of being selected for the sample (Joubert & Katzenllenbogen 2007: 95-96).

### **3.4 STUDY POPULATION**

When conducting a study, it is important to define clearly the group about which we want to gather information and draw conclusions. This group called the study (target) population should be clearly defined in respect of person, place and time as well as other factors relevant to the study (Joubert, et al 2007:94). Population is the collection of persons, objects or things that fulfil certain criteria set by the researcher for inclusion in the study where the researcher has a reasonable access (Burns & Grove 2005:40).

In this study, the study population comprised all TB patients confirmed to be MDR and non MDR-TB registered in 26 health centres in Addis Ababa from January 2008 to December 2011 meeting the following inclusion criteria:

#### **3.4.1 Inclusion criteria**

- MDR-TB confirmed by culture and drug sensitivity test.
- Any age of confirmed and registered to be MDR-TB and non MDR-TB among the health centers in Addis Ababa.
- Registered between January 2008 to December 2011 for both MDR-TB and non MDR-TB
- Either AFB, clinical or radiological evidence of sensitive tuberculosis for non MDR-TB.

### **3.4.2 Exclusion criteria**

- Patients whose registries were not found in the health center or information on the register was incomplete for the variables of interest.
- Being XDR-TB patient.

### **3.5 SAMPLE SIZE**

Saks and Allsop (2007:158) state that the larger the sample size, the smaller the error will be in estimating the characteristics of the whole population, but the more it will cost to administer a survey and analyse the data. The sample size is dependent on the accuracy required and the likely variation of the population characteristics being investigated.

The number of MDR-TB and non MDR-TB registered in the 26 public health centres in Addis Ababa between January 2008 and December 2011 and fulfilling the selection criteria were selected using systematic sampling method. Risk of exposure to MDR-TB among newly confirmed TB patients was taken as an indicator variable in order to estimate the minimum number of cases that need to be sampled for the study. According to the Federal MOH of Ethiopia, the risk of MDR-TB among newly confirmed TB patients is nearly 2% compared to 12% among re-treated TB patients (FMOH 2009:3).

A Fleiss with Continuity Correction sample size calculation formula using Open Epi version 2.3 for windows were used to calculate the sample size. A marginal

error of 3%, 80% study power, 95% confidence limit and a ratio of exposed (MDR) to un-exposed (non MDR) of 1:3 were assumed. Accordingly, a total of 400 study participants (100 MDR-TB and 300 non MDR-TB) are assumed to be included in this study. 10% of the samples were added to cater for incomplete data making the total sample size of 439 (113 MDR-TB and 326 non MDR-TB).

### **3.6 RESEARCH SETTING**

The study was conducted in Addis Ababa, the capital city of Ethiopia. It is divided into ten sub cities and 110 woredas (the lowest administrative units). During the data collection of this study only 26 public health centres were providing MDR-TB treatment and follow up services whose conditions are stable after refereed from St. Peter specialised hospital in Addis Ababa.

### **3.7 DATA COLLECTION**

The process by which values are obtained for the characteristics of individuals being studied (Joubert, et al 2007: 106). Data collection is the gathering of all the pertinent information necessary to answer a particular research question or hypothesis (Stommel & Wills 2004:363).

The data collection instrument was designed to abstract data from patient record - the TB registers. Data abstraction instrument was piloted in a selected health centre before the actual data collection took place. Data abstractors were focal TB nurses in each of the 26 public health center who are familiar with TB registers. They were trained to abstract data and the principal investigator did the quality control check. A total of two days training was given for supervisors and data collectors. The quality of the data was ensured throughout instrument development, data entry and analysis.

#### **3.7.1 Research instrument**

A research instrument is used to measure a variable of interest (Bowling 2002:144). (Joubert, et al 2007: 106) review of records much potentially useful health relate information is collected routinely as part of patient care, for example, for each patient who visits clinic. A research instrument is used to measure a variable of interest (Bowling 2002:144).

The abstraction form was developed based on the Ethiopian standardized national TB register and after review of literature and consultation of TB focal persons and programme managers. The checklist comprised the following sections:

Section I: Socio-demographic characteristics

Section II: TB treatment status, category and outcome

Section III: TB treatment adherence

Section IV: TB/HIV co-infection status

### **3.8 DATA ANALYSIS**

Polit and Beck (2008:507) identified the purpose of data analysis is to organize, provide structure to, and elicit meaning from research data. Trochim (2006:101) explained that in most social research, data analysis involves three major steps, namely cleaning and organising the data for analysis, describing the data, and testing hypotheses and models. De Vos, et al (2007:218) describe data analysis as the process of categorizing, putting into order, manipulating and ultimately summarizing data in order to be able to answer the original research questions.

The data were coded and entered in to Epi-Info (version 3.5) and exported to SPSS version 16.0. Odds ratio, Chi-square test, and logistic regression were calculated for inferential statistics and tables, graphs, charts, and percentages were used for descriptive statistics

### **3.9 VALIDITY AND RELIABILITY**

Validity and reliability are concerned with the quality of the data and appropriateness of the methods used in carrying out the study.

### **3.9.1 Validity of research instrument**

Polit and Beck (2007:196) defines Validity-the soundness of the study evidence-that is, whether the findings are unbiased, cogent and well grounded. It is whether there is evidence to support the assertion that the methods are really measuring the abstract concept that they purport to measure. Validity refers to the instrument's accuracy to measure the characteristics or attributes that it intends to measure (Stommel & Wills 2004:222).

To maintain the validity of the study, conceptual and operational definitions of terms were used according to the objective of the study. Records that meet eligibility and exclusion criteria based on clinical and laboratory results confirmed diagnosis will be selected. Pre-tested data abstraction forms were used. The data was stratified for age and gender and multivariate analysis were employed during the analysis. Consultation with medical officers and nurses providing medical service for TB patients were done to measure the construct domain of the study to ensure instruments validity.

### **3.9.2 Reliability of research instrument**

Reliability refers to the accuracy and consistency of information obtained in the study (Polit and Beck 2008:196). Reliability is the reproducibility and consistency of a measurement instrument's ability to produce results that are consistent across persons and time (Stommel & Wills 2004:209). To maintain the reliability of the study, careful training, development of a clearly defined standardized format after reviewing the literature, pre testing of the abstraction instrument and consulting experts in the field were designed and a small number of research assistants were used to enhance the accuracy of observer ratings and classifications. Only the researcher was responsible for cleaning abstracted data during conducting of the actual research and by so doing increased the chances of consistency collected data.

### **3.10 ETHICAL CONSIDERATIONS**

In order to ensure the rights of study participants are not violated, researchers have to adhere to strict ethical standards (Burns & Grove 2005:176). The Principle of Beneficence" requires the researcher to "do good and above all, do no harm" (Burns & Grove 2005:180). The primary ethical principles on which standards of ethical conduct in research are based: beneficence, respect for human dignity and justice (Polit & Beck 2008: 170-174).

#### **3.10.1 Protection of human rights:**

The human rights that require protection in research are:

- Right to self determination
- Right to privacy
- Right to anonymity and confidentiality
- Right to fair treatment
- Protection from harm and discomfort (Burns and Grove 1999:196)

This study involves review of patient records. It did not involve direct contact with human beings thus no potential for inconveniencing patients by providing personal information. Nonetheless, all the necessary ethical precautions to protect privacy and confidentiality of personal information have been observed. Names and addresses of patients were not included in the abstracted information (de-identification). Data was kept in locked cabinets and password protected computers during data processing and analysis.

#### **3.10.2 Informed consent:**

Informed consent is not applicable for this study because the study did not have direct interaction with patients as it used secondary data.



### **3.10.3 Autonomy:**

In this study, data was abstracted from medical records and hence there is no direct interaction with the patients. Authorities act on behalf of the patients, autonomy of the participant were maintained through approval by facility authorities for undertaking the study. Authorities at the study sites were asked to specify their own restriction on the access to and use of their data.

### **3.10.4 Confidentiality and anonymity:**

For this study, patient personal identifiers (such as name and address) were removed from abstraction to ensure anonymity of data while maintaining the integrity of the medical records. The collected data was stored in locked cabinets and secured databases. The access to the abstracted data was limited to the researcher and those who were involved in analysis of the data were limited. The researcher also informed all the facility authorities that although the data obtained from the health records might be reported in scientific journals, no information would ever be disclosed that will enable any third party to identify them as participants in the research.

### **3.10.5 Beneficence:**

The researcher did not directly interact with the patients. The facility authorities were informed that the benefits of this study outcome outweigh the risks to the study participants by contributing to the existing body of scientific knowledge by identifying the risk factor for lethal diseases of MDR-TB.

### **3.10.6 Justice:**

*Risk/benefit ratio*-there was no risks of exposing the respondents to discomfort or harm as there is no direct interaction with the patients. But potential benefit of the study is to contribute the existing body of knowledge about MDR-TB in determining the risk factor.

### **3.10.7 Rights of institutions where the research is based:**

Prior to conducting the study, ethical clearance was sought from the University of South Africa (UNISA) postgraduate research and ethics committee. Authorised cooperation letter were written from UNISA regional learning centre to Addis Ababa City Administration Health Bureau (AACAHB). A request for permission letter having detailed explanation of the research itself, the reasons for the research and kind of research that would be conducted in the facility were approved by AACAHB and the authorities at the study sites. Authorities at the study site were assured that any information that the researcher will come across during the conduct of the research will not be divulged to any interest groups that could jeopardize the patient's welfare in society and the concerned institution. The researcher abided by the guideline of the institutions, which has the right to terminate the study if the safety and confidentiality of patients' records are compromised.

### **3.10.8 Scientific integrity on the part of the researcher:**

To maintain scientific integrity and eliminate the possibility of scientific misconduct and plagiarism, the researcher strictly adhered to ethical and appropriate use of scientific knowledge by refrain from falsifying or fabricating primary and secondary data. The information obtained from patient records' were recorded as such. Clear reference was given to the respective source when citing ideas, words, processes, findings and results obtained by other authors, and important results which are contrary to the researcher's results and conclusions.

## **3.11 CONCLUSION**

This chapter described the research design and methodology, including the population, data collection and analysis, validity and reliability, and ethical considerations. Chapter 4 presents the data analysis and interpretation.

## CHAPTER 4

### Analysis and discussion of the research findings

#### 4.1 INTRODUCTION

In the previous chapter, the research design and methodology was described. This chapter presents the results with the aid of percentages, tables and graphs. The purpose of the study was to investigate the risk factors for MDR-TB in Addis Ababa, Ethiopia in order to add to the paucity of knowledge in this area of public health.

The specific objectives of the study were to:

- To determine the socio-demographic factors associated with MDR-TB among patients in Addis Ababa.
- To determine if non adherence to treatment is associated with development MDR-TB.
- To determine the types of TB treatment categories and treatment outcomes associated with MDR-TB.
- To determine the association of HIV/AIDS and MDR-TB in Addis Ababa.

#### 4.3 DATA MANAGEMENT AND ANALYSIS

Medical record of 439 patients was analysed - 113 MDR-TB cases and 326 non MDR-TB patients. All MDR-TB patients registered at 26 public health centres in Addis Ababa between January 2008 and December 2011 were included and the number of matching non MDR-TB patients from each health centre was decided using systematic random sampling technique. The data was at all times kept safely and stored in a place to which no one other than the researcher had access, and the data was saved and protected on by a secret password.

MDR-TB and non MDR-TB patients were compared on key socio-demographic and patient related factors (potential risk factors) for drug resistance. Initial descriptive analyses of all variables of interest were performed. Statistical

inference was made at 95% confidence limit. Univariate analysis was carried out in order to identify potential risk factors associated with drug resistance in TB treatment. The strength and magnitude of associations were estimated for each variable from the corresponding univariate model and expressed in terms of an odds ratio. Subsequently, multiple regression analysis was carried out with the set of variables that showed strong association in the univariate model. Maximum effort was used to include the potential risk factors for drug resistance in the model with multivariate setting.

A statistician assisted in data entry using Epi Info version 3.5 and analysis by exporting data to the Statistical Package for the Social Science (SPSS), version 16.0, and micro-computer program. The data analysis was discussed in accordance with the sections of the checklist.

## 4.4 RESEARCH RESULTS

### 4.4.1 Socio-demographic characteristics

This section covers description of study population's background by characters such age, gender, and geographical location of residence.

**Table 4.1: Socio-demographic data of the patients (n=439)**

Characteristics		MDR-TB patients (n= 113)	non MDR-TB patients (n= 326)	Crude OR (95% CI)	p-value
Gender:					
	Male	73 (65%)	166 (51%)	1.8 (1.13-2.74)	0.012
	Female	40 (35%)	160 (49%)		
Age:					
	5-14	2 (2%)	15 (5%)	0.3 (0.05-1.801	0.293
	15-24	36 (32%)	99 (31%)	0.8 (0.26-2.46)	0.800
	25-34	36 (32%)	100 (31%)	0.79 (0.25-0.4)	0.792
	35-44	16 (14%)	54 (17%)	0.65(0.197-2.2)	0.652
	45-54	11 (10%)	29 (9%)	0.8(0.236-2.96)	0.834
	55-64	7 (6%)	16 (5%)	0.963 (0.24-3.829)	0.0963
	≥65	5 (4%)	11 (3%)	1.00	
Geographical location:					
	Urban	103 (91%)	258(79%)	2.7 (1.35-5)	0.005
	Rural	10(9%)	68 (21%)	1.00	

#### **4.4.1.1: Sex distribution**

Of the total, 54% (n=239) were males and 46% (n=200) were females. Among the males, 65% (n=73) were MDR-TB patients and 51% (166) were non MDR-TB patients (OR: 1.8; 95% CI: 1.13-2.74), while of the females 35% (n=40) were MDR-TB patients and 49% (160) females were non MDR-TB patients (OR: 0.56; 95% CI: 0.36-0.86). Multivariate analysis demonstrated that male gender is associated with acquiring MDR-TB (OR 2; 95% CI 1.035-5).

#### **4.4.1.2: Age distribution**

The youngest TB subject was 5 years old, while the oldest TB subject was 77 years old. The median age was 29 years (SD of 14). More than 60% of both MDR and non-MDR patients were 15-34 years old. There was no statistically significant age difference between MDR and non-MDR patients.

#### **4.4.1.3: Geographical location of residence**

362 (82.2%) were urban residents whereas 78 (17.8%) came from rural geographical locations. Urban residents made up 91% (103) of the MDR-TB patients and 79% (259) among non MDR-TB patients (OR: 2.75; 95% CI: 1.35-5.00). Similarly, 9% (10) of the MDR-TB and 21% (68) of the non MDR-TB patients were coming from rural part of the country. The proportion of urban resident MDR-TB patient seems to be much greater than those of rural residents. But, during multivariate analysis urban residence is not associated with acquiring MDR-TB (OR=1.6; 95% CI: 0.5-5).

#### **4.4.2: TB treatment adherence status**

##### **4.4.2.1: Missed a dose of anti-TB drugs during intensive phase of previous treatment**

Of 99 MDR-TB and 28 non MDR-TB patients who had history of previous TB treatment, 11% (11) of MDR-TB and 18% (5) of non MDR-TB patients respectively missed dose of TB during intensive phase. 16% (16) of MDR-TB cases and 36% (10) of non MDR-TB patients didn't miss anti-TB treatment during intensive phase of previous treatment. But information on missed medication during intensive TB treatment period was unknown by far more MDR-TB patients 73% (72) compared to non-MDR TB patients 46% (13).

#### **4.4.2.2: Previous TB treatment adherence status of the patient**

91% (10) of the MDR-TB and 20% (1) of the non MDR-TB patients missed to pick  $\geq 20\%$  of their monthly dose ( $X^2$  test,  $p=0.005$ ). 9% (1) of MDR-TB and 80% (4) non MDR-TB patients missed  $<20\%$  of their monthly medications. There is significant association between acquiring MDR-TB and poor adherence to TB treatment.

#### **4.4.3: TB treatment status, category and outcome**

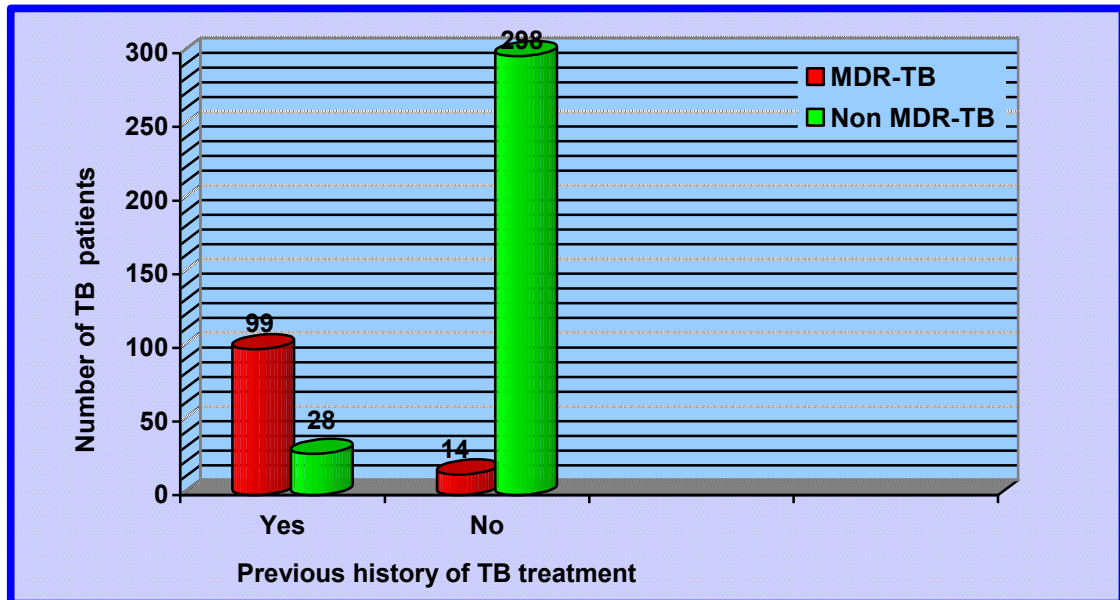
##### **4.4.3.1: Previous history of TB treatment**

**Table 4.2: Previous history of TB treatment status of MDR-TB (n=113) and non MDR-TB (n=326)**

Characteristics		MDR-TB patients (n=113)	Drug sensitive TB (n=326)	Crude OR (95% CI)	p-value
Previous history of TB treatment:					
	Yes	99 (88%)	28 (9%)	75 (38-148 )	0.00
	No	14 (12%)	298 (91%)	1.00	

Among the MDR-TB patients, 88% (99) have previously been treated for TB in comparison to 9% (28) of the non-MDR group (OR 75; 95% CI 38-148). Over 90% (298) of the non-MDR group had no history of previous TB treatment compared to 12% (14) of the MDR group (OR 0.013; 95% CI 0.007-0.026). Similarly, during multivariate analysis strong association is shown between previous history of TB treatment and risk of becoming ill with MDR-TB (OR 112;

95% CI 47-267).The finding of this study showed that those with history of previous TB treatment were 112 times more likely to become ill with MDR-TB in comparison to those who had no previous history of TB treatment.



**Figure 4.1 History of previous TB treatment in MDR-TB (n=113) and non MDR-TB (n=326)**

#### 4.4.3.2: Previous category of TB treatment

**Table 4.3: TB treatment category, frequency and outcome among those previously treated MDR-TB (n=99) and non MDR-TB (n=28)**

Characteristics	MDR-TB patients (n=99)	Drug sensitive TB (n=28)	Crude OR (95% CI)	p-value
Previous category of TB treatment:				
Failure	19 (19%)	6 (20%)	3.167 (0.36-27)	0.297
Relapse	6 (6%)	15 (54%)	0.4 (.05-3.5)	0.409
Return after default	2 (2%)	1(4%)	2 (0.09-44)	0.661
Failure after re-treatment	70 (70%)	5 (18%)	17 (2-158)	0.011
Not known	2 (2%)	1 (4%)	1.00	
Number of times the patient used anti-TB drugs:				
≥2 times	89 (90%)	13 (46%)	10 (3.8-27)	
Once	10 (10%)	15 (54%)	1.00	0.000
Outcome of previous treatment:				
Failure	90 (91%)	6 (21%)	36 (7-187)	0.00
Defaulted	6 (6%)	17 (61%)	0.7 (0.13-3.7)	0.683
Treatment completed	3 (3%)	5 (18%)	1.00	

Failure after re-treatment constitutes 70% (70) among MDR-TB patients and 18% (5) for non MDR-TB patients respectively (OR 17; 95% CI: 2-158). Failure of first time TB treatment constitutes 19% (19) for MDR-TB and 20% (6) for non MDR-TB patients, 6% (6) of MDR-TB and 54% (15) of non MDR-TB patients were categorised as relapse, and return after default constitutes 2% (2) of MDR-TB and 4% (1) of non MDR-TB. Result of multivariate analysis showed, TB treatment category of failure after re-treatment is strongly associated with becoming ill with MDR-TB (OR 31; 95% CI 11-63).

This result shows that those patients who failed after re-treated for TB were 31 fold at risk of becoming ill with MDR-TB in comparison to other category of TB treatment.

#### ***4.4.3.3: Number of times treated for TB***

Of all MDR-TB patients' 90% (89) MDR-TB patients were treated more than twice for tuberculosis in comparison to 46% (13) of non MDR-TB patients (OR 10; 95%CI 3.8-27). Multivariate analysis of the variable showed, those who received TB treatment more than two times were higher risk of becoming ill with MDR-TB (OR=1.7; 95% CI 1.03-34). From this result, frequency of TB treatment was strongly associated with developing MDR-TB.

#### ***4.4.3.4: Previous TB treatment outcome***

Of all MDR-TB patients 91% (90) had failure as TB treatment outcome compared to 21% (6) among non MDR-TB patients (OR 36; 95% CI 7-187). The remaining 6% (6) of the MDR and 61% (17) of the non MDR-TB patients had defaulted from previous treatment (OR 0.7; 95% CI 0.13-3.7). During multivariate analysis strong association is demonstrated between TB treatment outcome of failure and further risk of acquiring MDR-TB (OR 29; 95% CI 1.93-6). From this finding there is strong association between TB treatment failure and risk of becoming ill with MDR-TB.



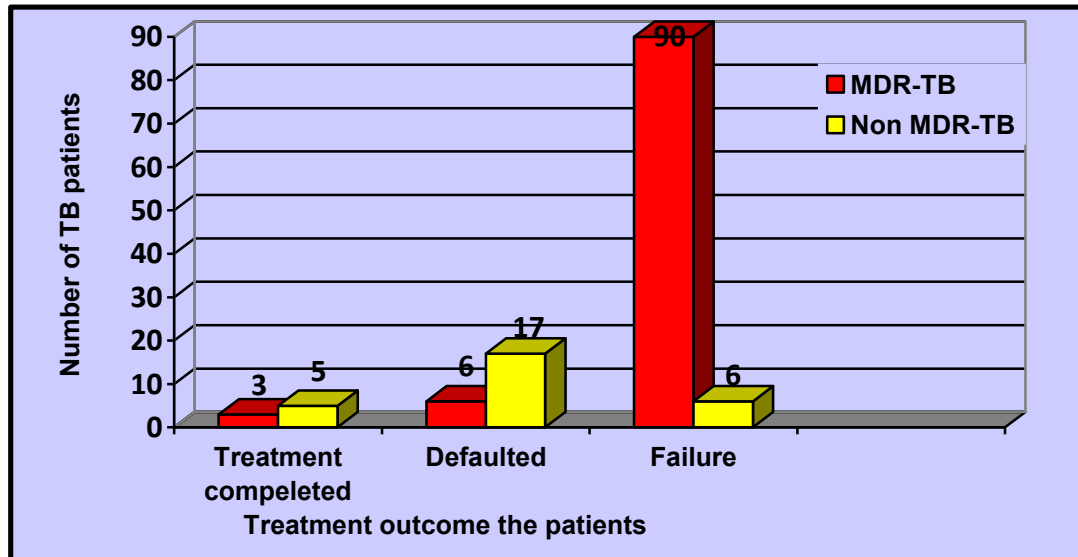


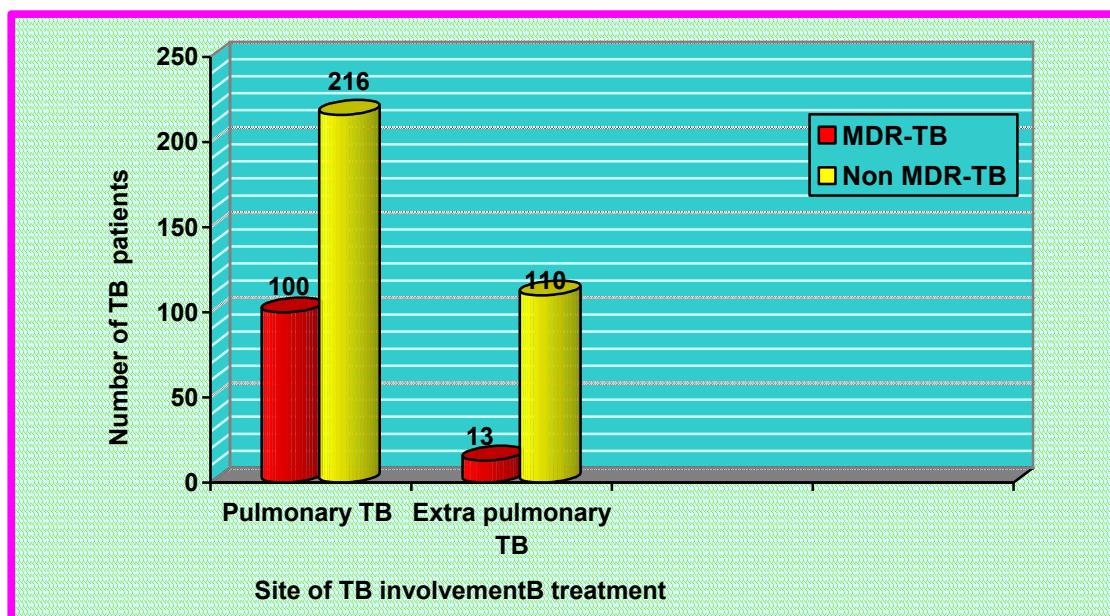
Figure 4.2 TB treatment outcome in previously treated MDR-TB (n=99) and non MDR-TB (n=28)

#### 4.4.3.5: Site of TB involvement

Table 4.4: Site of TB involvement among MDR-TB (n=113) and non MDR-TB (n=326)

Characteristics	MDR-TB patients (n=113)	Drug sensitive TB (n=326)	Crude OR (95% CI)	p-value
Site of TB involvement:				
Pulmonary	100(88.5%)	216 (66%)	3.9 (2-7.3)	0.00
Extra-pulmonary	13 (11.5%)	110 (34%)	1.00	
Result of Acid Fast Bacilli (AFB) smear for current TB treatment:				
Positive	89 (79%)	132 (40.5%)	5.5 (3.3-9)	0.00
Negative	24 (21%)	194 (59.5%)	1.00	

Big majority of TB infections, 88.5% (100), were pulmonary TB among the MDR-TB patients compared to 66% (216) among non MDR-TB (OR 4; 95% CI 2-7.3). The sites involved in 11.5% (13) of MDR-TB were extra pulmonary compared to 34% (110) among non MDR-TB patients (OR 0.26; 95% CI 0.14-0.5). Significant association between becoming ill with MDR-TB and pulmonary involvement of TB were demonstrated during multivariate analysis (OR 2; 95% CI 6-23).



**Figure 4.3 Site of TB involvement for MDR-TB (n=113) and non MDR-TB (n=326) patients**

#### 4.4.3.6: Result of Acid Fast Bacilli (AFB) smear

From this study 79% (89) of MDR-TB and 40.5% (132) non MDR-TB were smear positives (OR 5.5; 95% CI: 3.3-9), 21% (24) of MDR-TB and 59.5% (194) of the non MDR-TB were smear negative pulmonary TB. Significant association between becoming ill with MDR-TB and positive AFB smear were demonstrated during multivariate analysis (OR 8; 95% CI 3.5-19). From this result of study, MDR-TB patients are 8 times more likely present with smear positive in comparison to non MDR-TB patients.

#### 4.4.4: HIV status of the MDR-TB and non MDR-TB patients

**Table 4.5: HIV status of study participants in MDR-TB (n=113) and non MDR-TB (n=326)**

Characteristics	MDR-TB patients (n= 113)	Non MDR-TB (n= 326)	Crude OR (95% CI)	p-value
Result of HIV test:				
Positive	54 (48%)	85 (26%)	3 (2-4)	0.00
Negative	59 (52%)	241 (74%)	1.00	

#### 4.4.4.1: TB/HIV co-infection

Almost half, 48% (54) of MDR-TB and 26% (85) of non MDR-TB patients were HIV positive (OR 2.6; 95% CI 1.7- 4). Strong association between becoming ill with MDR-TB and HIV positive were demonstrated during multivariate analysis (OR 3; 95% CI 1.2-5.6). The risk of becoming ill with MDR-TB is 3 times higher among TB/HIV co-infected individuals.

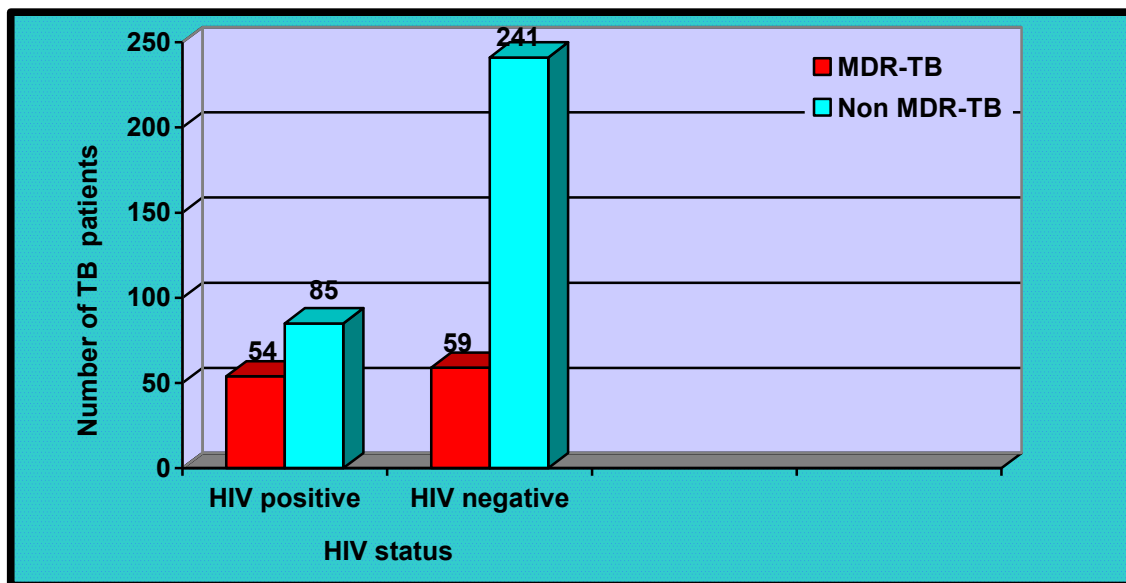


Figure 4.4 HIV status of MDR-TB (n=113) and non MDR-TB (n=326)

Table 4.6: Socio-demographic characteristics and patient related factors of MDR and non MDR-TB patients (n=439)

Characteristics		Crude OR (95% CI)	p-value	Adjusted OR <sup>a</sup> (95% CI)	p-value
Gender:					
	Male	1.76 (1.13-	0.012	2 (1.035-5)	0.039
	Female	2.74)		1.00	
Geographical location of residence:					
	Urban	2.7 (1.35-5.5)	0.005	1.6 (0.5-5)	0.396
	Rural	1.00		1.00	
Previous history of TB treatment:					
	Yes	75(38-148)	0.00	112 (47-267)	0.00
	No	1.00		1.00	
Number of times TB treatment used:					
	Once	1.00		0.00	
	≥2 times	10 (3.8-27)	0.00	1.7 (1.03-34)	0.024
Previous category of TB					

treatment:					
Failure of first treatment	3.17 (0.36-27)	0.297	0.29 (0.91-7)	0.741	
Relapse	0.4 (0.05-3.5)	0.409	0.23 (0.15-8.1)	0.260	
Return after default	2 (0.09-44)	0.661	19 (0.31-103)	0.29	
Failure after re-treatment	17 (2-158)	0.011	31 (11-63)	0.003	
Not known	1.00				
Outcome of previous treatment:					
Failure	36 (7-187)	0.00	29(1.93-6)	0.00	
Defaulted	0.7 (0.13-3.7)	0.683	1.7(0.29-0.973)	0.871	
Treatment completed	1.00		1.00		
Site of TB involvement:					
Pulmonary	3.9 (2-7.3)		2(6-23)	0.00	
Extra-pulmonary	1.00	0.00	0.00		
Acid Fast Bacilli (AFB) smear for current TB treatment:					
Positive	5(3.3-9)	0.00	8 (3.5-19)	0.000	
Negative	1.00				
Result of HIV test:					
Positive	2.6(1.7- 4)	0.00	3 (1.2-5.6)	0.012	
Negative	1.00		1.00		

<sup>a</sup>The data were analysed using bi-variate and multivariate logistic regression.

Each odds ratio has adjusted for all other characteristics in the table.

OR-odds ratio, CI-confidence interval

In conclusion, bivariate analysis and subsequent multivariate analysis of male gender, two or more times previous history of TB treatment, previous category of failure after re-treatment, failed TB treatment outcome, sputum smear positive pulmonary TB and being HIV positive were significantly associated with the risks of becoming ill with MDR-TB.

## 4.5 CONCLUSION

This chapter discussed the data analysis and interpretation of the findings with reference to the literature review where needed. The results were presented in tables and figures.

Chapter 5 concludes the study by discussing the limitations and makes recommendations for practice and further research.

## CHAPTER 5

### Conclusions, limitations and Recommendations

#### 5.1 INTRODUCTION

The purpose of this study was to investigate the risk factors for MDR-TB in Addis Ababa, Ethiopia. Data on risk factors contributing for the occurrence of MDR-TB can be used in designing educational messages that can improve health care seeking towards MDR-TB. The findings could provide important information on ways to improve quality of MDR-TB care in the country.

#### 5.2 RESEARCH DESIGN AND METHODOLOGY

Tuberculosis (TB) is one of the leading causes of morbidity, the fourth causes of hospital admissions, and the second cause of hospital deaths in Ethiopia (FMOH 2009: 1). The Ethiopian government policy makes provision for free care to TB patients, including consultation, laboratory services and non-payment for drugs. Despite these services the public health concern of MDR-TB is raising in the country, factors underlying for spread of this diseases is not yet determined. The study aims to investigate the risk factors for MDR-TB. The researcher adopted a quantitative approach, using a comparative cross-sectional study design to investigate the risk factors for emerging public health problem of MDR-TB in Addis Ababa.

The study population comprised MDR-TB and non MDR-TB patients who were registered between January 2008 to December 2011 and taking their treatment in 26 public health centres in Addis Ababa. A total of 439 medical records of TB patients were included in this study, 113 MDR-TB and 326 non MDR-TB patients. Data were transcribed from each TB patient's medical records using a specifically designed checklist.

### **5.3 SUMMARY AND INTERPRETATION OF THE RESEARCH FINDINGS**

The findings are discussed according to the 4 objective of the study. The specific objectives of the study were to:

- To determine the socio-demographic factors associated with MDR-TB among patients in Addis Ababa.
- To determine if non adherence to treatment is associated with development MDR-TB.
- To determine the types of TB treatment categories and treatment outcomes associated with MDR-TB.
- To determine the association of HIV/AIDS and MDR-TB in Addis Ababa.

#### **5.3.1: To determine the socio-demographic factors associated with the risk of MDR-TB**

##### ***5.3.1.1: Socio-demographic factors of MDR-TB and non MDR-TB patients***

###### ***5.3.1.1.1: Gender as a risk factor for MDR-TB***

The result showed that MDR-TB is more common among men. These results are similar to those that were reported by Molly et al (2008:4) in a study carried out in Peru. Stronger association of being a male sex as a risk factor for MDR-TB is found in other studies such as those undertaken by Faustini et al (2006:161). WHO (2010:12) corroborate male gender was associated with the risk of becoming ill with MDR-TB.

Muayad et al (2011: 517) described the higher prevalence of MDR-TB in men over women may be explained by the fact that women are more compliant with treatment and therefore less likely to receive inadequate treatment than men. Furthermore, men are almost always outdoors and therefore more susceptible to community-acquired resistant strains.

###### ***5.3.1.1.2: Age as a risk factor for MDR-TB***

More than 60% of both MDR and non-MDR patients were 15-34 years old. There was no statistically significant age difference between MDR and non-MDR patients. But the concentration of MDR-TB is shown to be high among young adults aged 15-34 years. Similarly the highest toll of MDR-TB is shown in a report of study by W. S. Law et al (2008:1065) including WHO (2010:4), i.e., younger age was found to be the significant contributor for development of MDR-TB. Waseem et al (2009:21)) showed seventy-two percent of the MDR-TB patients were young men with mean age of  $32.28 \pm 8.7$  yrs. But, similar study conducted in South Africa, Scott et al (2010:3) showed that age was not a significant risk factor.

#### *5.3.1.1.3: Role of geographical location of patients in relation to health facilities*

The results of this study showed that there is no association between geographical location of residence of being urban or rural and risk of becoming ill with MDR-TB. But in Georgia, Vashakidze et al (2009: 5) found living in densely populated capital city were risk factor for becoming ill with MDR-TB.

### **5.3.2: To determine if non adherence to treatment is associated with development MDR-TB**

#### **5.3.2.1: TB treatment adherence status**

There was significant association between acquiring MDR-TB and non-adhering to TB treatment. These results are similar to the study reported by W. S. Law et al (2008: 1066).

There is significant association between acquiring MDR-TB and missing TB medication during intensive phase. This study suggests that there is a need to improve the knowledge of patients on TB treatment adherence to reduce the occurrence of MDR-TB. Besides there were a large percentage of records with unknown treatment outcome status among MDR-TB patients, indicating inadequate record-keeping practices by some healthcare providers. This might have also resulted from high rate of treatment defaulting among these patients.

### **5.3.3: To determine the types of TB treatment categories and outcomes associated with MDR-TB**

#### ***5.3.3.1: Previous history of TB treatment***

There was a significant association between previous history of TB treatment and the risk of becoming ill with MDR-TB. In Estonia, Kiliman (2009:64) also found previous history of TB treatment as significant contributor for occurrence of MDR-TB. According to Kai et al (2009: 770), Alistair et al (2010: 268) and WHO (2010:10) discloses patients who received previous anti-tuberculosis treatment had a 4-fold increased odds of acquiring multidrug resistance and prior exposure to anti-TB drugs is a well-established risk factor for drug resistance.

#### ***5.3.3.2: Previous category of TB treatment***

There was a significant association between acquiring MDR-TB and previous treatment outcome of failure after re-treatment. Patients who fail after re-treated for TB were 31 fold riskier in developing MDR-TB relative to other treatment categories (those who failed after first time treatment, those who returned after defaulting and those with relapse). This supports the findings in a study conducted by D'souza et al (2009: 9), which found strong association of MDR-TB in those fails TB re-treatment. This suggests a need for clear medication guide and provision constant reminders for patients during their DOTs to prevent acquisition of MDR-TB. Similarly, priority should be given for routine DST among TB retreatment cases to make early diagnosis of MDR-TB.

#### ***5.3.3.3: Number of times treated for TB***

There was strong statistical association between frequency of TB treatment and the risk of developing MDR-TB. Those patients who were treated for TB more than two or more times were 1.7 times more likely to be at risk of developing



MDR-TB in comparison to those who were treated less frequently. This might be due to high chances of defaulting of TB patients from treatment. This result is similar with the finding of Waseem et al (2009:21). In Pakistan, Fazli et al (2009: 163) found 20% of the MDR-TB patients used anti-TB treatment course once, 53.3% twice and 26.7% three times in the past and 80% used twice or more times.

#### **5.3.3.4: Previous TB treatment outcome**

91% (90) of MDR-TB had failure TB treatment outcome compared to 21% (6) among non MDR-TB patients. The remaining 6% (6) of the MDR and 61% (17) of the non MDR-TB patients had defaulted from previous treatment. This shows a strong association between TB treatment failure and risk of becoming ill with MDR-TB. Those patients who were previously failed their treatment were 29 times more likely to develop MDR-TB in comparison to those who were not failed their TB treatment. In Republic of South Africa, Andrews et al (2010:4) found MDR and XDR-TB were strongly associated with a history of TB treatment failure.

#### **5.3.3.5: Site of TB involvement**

Based on these findings, it is plausible to assume that pulmonary involvement of TB is associated more with MDR-TB. Among thus, smear positive pulmonary TB patients were 2 times more likely to develop MDR-TB in comparison to smear negative pulmonary TB patients. Similarly, the study conducted in Hong Kong, China by S. Law et al (2008: 1066) showed vast majority of MDR-TB cases suffered from pulmonary TB (PTB) (98%). The study conducted in Tomsk, Russian Federation, Gelmanova et al (2007:705) discloses that sputum-smear positivity was significantly associated with MDR-TB.

#### **5.3.4.1: TB/HIV co-infection**

There was strong association between TB and HIV co-infection and the risk of becoming ill with MDR-TB. TB/HIV co-infected patients in this study are 3 times

more likely to have MDR-TB infection than treatment sensitive TB or non MDR-TB patients.

This supports the findings of Gandhi et al (2010:82), conducted in South Africa, where 90% of patients with MDR-TB were co-infected with HIV. In a similar vein, the report of a study by Scott et al (2010:3) and Suchindran et al (2009:4) shown high percentage of MDR-TB among HIV infected individuals and higher odds of harbouring MDR-TB strains than TB patients for whom HIV negative.

TB infected patients must be frequently screened for HIV and vice versa. ARV therapy should be initiated for all TB patients as soon as possible. A special attention must be given to selection of appropriate TB and ARV treatment regimens in order to avoid the risk of increased drug reaction and resistance.

In general, the study indicated that male gender, poor TB treatment compliance, previous history of TB treatment, previous history of failed TB treatment, pulmonary involvement of TB infection, and TB/HIV co-infection were associated with the risk of MDR-TB acquisitions.

#### **5.4 LIMITATIONS OF THE STUDY**

The study is limited by its cross-sectional design and use of secondary data for analysis. A further limitation is that these findings cannot be directly generalised to all regions other than Addis Ababa because of socio-economical, epidemiological and health system related variations in TB and MDR-TB occurrences.

The study does, however, provide important information about the common risk factors that influence the emergence of MDR-TB in Addis Ababa. This information would have critical benefit in TB patient education, improvement in quality of TB care and prevention of MDR-TB.

#### **5.5 RECOMMENDATIONS**

On the basis of the findings of this study, the researcher makes the following recommendations that might be useful for addressing the risk factors for MDR-TB that might be useful in actual practice and for further research.

#### **5.5.1 Practice**

- Effort should be increased to prioritise the development and implementation of effective MDR-TB screening and adherence to treatment protocols for those high risk groups to avoid the emergence of resistance. Patients with previous TB treatment history, those who had failure after re-treatment, those who developed TB treatment failure as an outcome, those who were treated for TB twice or more times, pulmonary TB cases, and TB/HIV co-infected individuals are some of the priority patient groups according to this study.
- Health education should be strengthened on TB treatment adherence. A checklist must be used to ensure that no vital information is omitted; for example, the duration of treatment, when to take their medications, how to recognise and handle side effects, and importance of TB treatment compliance to prevent further becoming ill with MDR-TB.
- Dedicated coordinators should be appointed to TB programs in health facilities. Frequent on-job trainings should be given for health care workers involved in TB management to improve recording and reporting.

#### **5.5.2 Further research**

Further research needs to be conducted on the following topics:

- A. National health system analysis to identify factors that favour the emergence of MDR-TB in Ethiopia.
- B. Review of the impact of HIV/AIDS on MDR-TB treatment outcome
- C. Case-control study to assess reasons why males are more at risk of becoming ill with MDR-TB

## **5.6 CONCLUSION**

This chapter concluded the study by discussing its limitations and by making a variety of recommendations on the basis of the results obtained from the study. These can be used to address the risk factors for MDR-TB and they can also be used in further research that addresses MDR-TB prevention and patient management with MDR-TB. The prevention of this lethal public health problem of MDR-TB requires combined effort of all stake holders, namely the government, the health care workers, patient and community to tackle the problem. The researcher is of the opinion that this study will contribute significantly to alleviating the problem of TB and identified risk factors for MDR-TB.

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**Annexures**

Annexure A- UNISA Ethical Clearance Letter

Annexure B- Permission Letter to Conduct the Research

Annexure C- Permission Letter from Addis Ababa City Administration Health

Bureau

Annexure D- Data Abstraction Tool